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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,085	04/12/2005	Zi-Hua Jiang	JIANG4A	3733

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EXAMINER	
NAVARRO, ALBERT MARK	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,085	JIANG ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68,72-81 and 100* is/are pending in the application.

4a) Of the above claim(s) *10,34 and 36-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-33,35,55-68,72-81 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/7/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-68, 72-81 and 100 in the reply filed on September 13, 2007 is acknowledged.

Applicants have traversed the species election of choices D, E, F, and J. The requirement for an election of DNA or RNA, a lipophillic group into a free end, as well as an internucleoside linkage which is not polyethyleneimine are all withdrawn. As suggested by Applicants, choice D should have properly offered a choice of DNA/RNA or an oligonucleotide at least part of whose backbone differs from that of DNA/RNA. Applicants election of DNA will be examined for both DNA and RNA.

Accordingly, claims 1-68, 72-81 and 100 are pending in the instant application, of which claims 10, 34, 36-51, and 53-54 are withdrawn from further consideration as being drawn to a non-elected species. Note, Applicants have not indicated claim 52 as withdrawn, however, claim 52 depends upon claim 51, drawn to non-natural internucleoside linkages. Applicants election of DNA/RNA excludes non-natural internucleoside linkages, accordingly, claim 52 is also withdrawn as a non elected species.

Accordingly, claims 1-9, 11-33, 35, 53-68. 72-81 and 100 are currently under examination.

Claim Objections

1. Claim 11 is objected to because of the following informalities:

Reference to Figures or Tables. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

Claim Rejections - 35 USC § 112

2. Claims 1 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "analogue thereof." One of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance what amount of derivation is allowed to still be considered an analogue? Similarly at what point is the molecule sufficient altered to no longer be considered an analogue? Without a clear definition as to the metes and bounds of the term analogue one of skill in the art would be unable to determine the metes and bounds of the claim.

3. Claims 4-5, and 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite in the recitation of "strongly/highly lipophillic." One of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance what level of lipophillic is considered strong? Similarly at what point is level no longer considered strong, but rather weak or even average? Without a clear definition as to the metes and bounds of the term strongly/highly lipophillic one of skill in the art would be unable to determine the metes and bounds of the claim.

4. Claim 66 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite in the recitation of "short/long internucleoside linkages." One of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance what length of internucleoside linkage is considered short? Similarly at what point is the internucleoside linkage no longer considered short but rather normal? Likewise, at what point does the average length internucleoside linkage become long? Without a clear definition as to the metes and bounds of the term short/long internucleoside linkage one of skill in the art would be unable to determine the metes and bounds of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-9, 11-14, 17-33, 35, 55-56, 59-63, 65-68, 72-81 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Polson et al.

The claims are directed to a method of stimulating the immune system of a subject which comprises administering to the subject an immunologically effective amount of an immunostimulatory molecule which comprises at least one oligonucleotide strand which comprises at least one oligonucleotide comprising a plurality of nucleotides, each nucleotide comprising a nucleobase, and thereby also comprising at least one CxG dinucleotide unit or analogue thereof, and at least one covalently incorporated lipophillic group.

Polson et al (US Patent 4,894,229) disclose of the oldest carrier bound immunogenic determinant materials known are complete bacterial cells. Polson et al further set forth that the immunogenic determinant of the bacteria is O-specific long chain polysaccharide immunogenic (antigenic) determinants covalently bonded to a lipophilic surface of the cell wall. (See summary).

Given that bacterial strains inherently comprise immunostimulatory molecules comprising at least one CxG molecule, as well as covalently incorporated lipophillic

groups, and that they have been administered as carriers for eliciting an immune response, the disclosure of Polson et al is deemed to anticipate the claimed invention.

6. Claims 1-9, 11-33, 35, 55-63, 65-68, 72-81, and 100 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Agrawal.

The claims are directed to a method of stimulating the immune system of a subject which comprises administering to the subject an immunologically effective amount of an immunostimulatory molecule which comprises at least one oligonucleotide strand which comprises at least one oligonucleotide comprising a plurality of nucleotides, each nucleotide comprising a nucleobase, and thereby also comprising at least one CxG dinucleotide unit or analogue thereof, and at least one covalently incorporated lipophillic group.

Agrawal (US Patent Number 5,856,462) disclose of modified CpG nucleotides administered to mammals. (See abstract), Agrawal further set forth that the term "oligonucleotide" encompasses polymers having chemically modified bases or sugars and/or having additional substituents, including without limitation ***lipophilic groups***. (Emphasis added, See column 4).

Accordingly, Agrawal is deemed to address each and every limitation set forth in the instantly filed claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-9, 11-33, 35, 55-68, 72-81, and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreig et al and Davis et al in view of Shea et al.

The claims are directed to a method of stimulating the immune system of a subject which comprises administering to the subject an immunologically effective amount of an immunostimulatory molecule which comprises at least one oligonucleotide strand which comprises at least one oligonucleotide comprising a plurality of nucleotides, each nucleotide comprising a nucleobase, and thereby also comprising at

least one CxG dinucleotide unit or analogue thereof, and at least one covalently incorporated lipophillic group.

Kreig et al (WO WO 98/18810) teach of nucleic acid sequences containing unmethylated CpG dinucleotides that modulate an immune response including stimulating a Th1 pattern of immune activation, cytokine production, NK lytic activity and B cell proliferation. (See abstract and claims)

Davis et al (WO 98/40100) teach of therapeutic methods for stimulating an immune response comprising administering at least one CpG dinucleotide and an antigenic polypeptide. (See abstract and claims).

Neither Kreig et al nor Davis et al teach of a covalently incorporated lipophilic group.

Shea et al (Nucleic Acids Research Vol. 18, No. 13, pp 3777-3783, 1990) teach of lipid-oligodeoxynucleotide conjugates which have antiviral activity. Shea et al further set forth that uptake experiments showed 8-10 times more lipid-DNA became more cell-associated than did unmodified DNA. (See abstract).

Given that Kreig et al and Davis et al have taught of CpG dinucleotides combined with antigenic polypeptides for stimulating an immune response, and that Shea et al have demonstrated that lipid-DNA complexes were 8-10 times more cell associated than unaltered DNA, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have taken the CpG dinucleotide/antigenic polypeptide composition for stimulating an immune response as taught by Kreig et al and Davis et al and to have incorporated a lipophilic group as taught by Shea et al. One

would have been motivated to produce such a molecule in view of the demonstrated increase in cellular uptake (8-10 fold) as reported by Shea et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shannon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
June 6, 2008